研究報文

中年の日本人における上下肢生体インピーダンス法による四肢の骨格筋量の正確な評価

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An accurate estimation of appendicular skeletal muscle mass by simple bioelectrical impedance method between the upper and lower limbs in middle-aged Japanese

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Summary

Objectives: This study aimed to develop a skeletal muscle mass prediction formula for the upper and lower limbs using bioelectrical impedance (BI) method, and to investigate the relation to the atherosclerosis risk factors.

Methods: This study was in two parts. First, a new device using the skeletal muscle mass prediction formula for the upper and lower limbs was developed using the data of 1197 healthy males and females in whom BI, height, weight, and skeletal muscle mass were measured. Dual energy X-ray absorptiometry (DXA) was used as the reference method. Second, using the device with the developed prediction formula, we measured BI, waist circumference, and the atherosclerosis risk factors in 1161 untreated males and females who underwent an annual medical check-up and investigated the association of the number of atherosclerosis risk factors and the skeletal muscle mass index (SMI).

Results: The correlation between the estimated skeletal muscle mass and DXA of the upper and lower limbs were 0.94 and 0.95, respectively ($P < 0.001$ for both). In males with a waist circumference less than the standard value (85cm), the number of atherosclerosis risk factors was significantly correlated with SMI of the lower limbs ($B = -0.109$, $P = 0.011$). The cutoff values of SMI of the upper and lower limbs for males and females as a predictor of the presence of at least two of the atherosclerosis risks factors were 8.4 kg/m^2 and 6.5 kg/m^2, respectively. These cutoff values were higher than the cutoff for sarcopenia (7.0kg/m^2 for males and 5.7kg/m^2 for females).

Conclusions: A new device using the skeletal muscle mass prediction formula for the upper and lower limbs with a high degree of accuracy. It is suggested that the decrease in skeletal muscle causes atherosclerosis earlier than sarcopenia in middle-aged Japanese.

(Received 4 October, 2019, Accepted 25 November)

1. Introduction

Sarcopenia is defined as the age-related decline in skeletal muscle mass [1]. It is well known that the cross-sectional area of skeletal muscle is decreased by 25%–30%, and the muscle strength is decreased by 30%–40% in individuals who are 70 years old compared with the people in their twenties. In addition, the muscle mass decreases at a rate of 1%–2% every year after the age of 50 years [2].

Currently, the recommended criteria for the diagnosis of sarcopenia requires documentation for low appendicular skeletal muscle mass (ASM) and low muscle strength or low physical performance [3, 4]. ASM is defined by the sum of the lean soft tissue mass from the four limbs [5]. Furthermore, the height-adjusted muscle mass was a more

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suitable skeletal muscle index (SMI) for assessing sarcopenia among Asian populations [6, 7]. Therefore, the SMI is calculated by the appendicular skeletal muscle mass divided by height (m) squared (ASM / height^2; kg/m^2); This equation was used in the current study on sarcopenia, for which the cutoff values of SMI, measured by BI method, are 7.0kg/m^2 for males and 5.7kg/m^2 for females [8].

In 2010, The European Working Group on Sarcopenia in Older People recommended using magnetic resonance imaging (MRI), computed tomography (CT), dual energy X-ray absorptiometry (DXA), and bioelectrical impedance analysis (BIA) as suitable methods for measuring muscle mass for sarcopenia research [3]. MRI and CT are the gold standards for estimating muscle mass in research. DXA and BIA are the preferred alternative method for research and clinical use. Therefore, ASM is commonly measured using DXA or BIA. BIA method is simple, easy, and does not involve radiation exposure to the subject. Several sarcopenia studies using BIA devices as diagnosis tools have been reported [9-13]; however, their methods for calculating ASM using BIA devices were not disclosed [14]. Due to the size of these devices, they are usually only used to measure ASM at medical institutions.

The previous studies have reported that the skeletal muscle mass is not only related to sarcopenia but also atherosclerosis risk [15, 16]. In an earlier paper, we reported that visceral fat area and skeletal muscle percentage are independent risk factors for atherosclerosis [17]. We developed a BIA device for measuring the SMI in the upper and lower limbs and examined the association between atherosclerosis risk and SMI as the clinical application of the device. Our study was conducted in two parts. The purpose of the first part of our study was to develop the formula to use with the new BI device for the prediction of lean soft tissue mass (LSTM) as skeletal muscle mass in upper limbs and lower limbs respectively using the BIA method in reference to LSTM of DXA within the guideline. The purpose of the second part of our study was to investigate the relationship between skeletal muscle mass in upper limbs and lower limbs and atherosclerosis risk.

2. Methods

2. 1. Study 1

2. 1. 1 Subjects

We enrolled 1,197 healthy Japanese adults aged 20−80 years (536 males and 661 females). The subjects were randomly separated into the validation group (268 males and 331 females) or the cross-validation group (268 males and 330 females) so that there were no significant age differences between the two groups.

2. 1. 2. Anthropometric measurements

The body weight of each subject was measured to the nearest 0.1 kg with the subject in light clothes, and the height was measured to the nearest 0.1 cm. From these measurements, the body mass index (BMI) and body surface area (BSA) were calculated [18].

2. 1. 3. Dual energy X-ray absorptiometry measurement

DXA measurements of LSTM were performed using a Lunar DPX-LIQ (Lunar Co., Madison, WI, USA; software version 4.7E). The subjects were scanned with their arms down and lying in the supine position. The total body scan took less than 15 minutes to complete.

2. 1. 4. Bioelectrical impedance measurement

Bioelectrical impedance (BI) was measured in the upper and lower limbs using the HBF-354 prototype (OMRON Healthcare Co. Ltd., Kyoto, Japan) [18]. The equipment used for impedance (Z) measurements included handgrips and footplate electrodes. Each electrode was connected to the main unit by cables.

The different types of Z measurements taken using this method included the following: whole-body Z between the upper and lower limbs (Zw), Z between right hand and left hand (Zh), and Z between right foot and left foot (Zf). Zw was determined by measuring the voltage induced by applying a current to electrodes fixed on the bilateral palms and soles while shorting each electrode with the bilateral palms and soles in the standing position and the upper limbs extended forward. A constant current of 500 μA at 50 kHz was applied. The three BI indices were calculated as height^2/Zw, height^2/Zh, and height^2/Zf.

2. 1. 5. Statistical analysis

All statistical analyses were performed using SPSS Statistics version 21 for Windows (IBM Corp., Armonk, NY). Data are presented as the mean ± standard deviation, and statistical significance was set at $P < 0.05$. We used the Mann-Whitney U test to assess significant differences between the groups, and Spearman's correlation coefficient to assess correlations between the two vari-

ables when the values were not normally distributed.

Stepwise multiple linear regression analysis was used to develop the prediction equation for determining LSTM of the upper and lower limbs using three BI indices, gender, age, height, body weight, BMI, and BSA as independent variables as described in our previous study [18].

The predicted values for LSTM were calculated for the individuals in the cross-validation group using the equations derived for the validation group. The differences between the DXA-measured and BIA-predicted LSTM measurements were determined using a paired t-test.

2. 2. Study 2

2. 2. 1. Subjects

We enrolled a total of 1441 adults (1250 males and 191 women; mean age ± SD, 50.3 ± 7.2 and 49.3 ± 8.8 years, respectively), who had undergone an annual medical check-up at a health check-up center in the Kinki area of Japan between February 2012 and April 2015. We excluded 252 males and 28 females that were taking antihypertensive agents, antidiabetic agents, and lipid-lowering agents, or who had dehydrative or edematous diseases. The final study included 1161 adults (998 males and 163 females; mean age ± SD, 49.4 ± 7.4 and 48.2 ± 8.9 years, respectively).

2. 2. 2. Anthropometric and atherosclerosis risk factor assessments

Each morning, the body weight of each subject was measured to the nearest 0.1 kg, with the subject in light clothes, and the height was measured to the nearest 0.1 cm. The waist circumference (WC) was measured by a well-trained examiner to the nearest 0.5 cm at the umbilical level during the late exhalation phase while the subject was standing. Blood pressure measurements were obtained in the morning while the subjects were resting in a seated position. Blood samples were collected, after an overnight fast, for assessment of fasting plasma glucose, triglyceride, and high-density lipoprotein (HDL)-cholesterol levels.

2. 2. 3. Diagnosis of atherosclerosis risk factors

We used hypertension, diabetes, and dyslipidemia as an assessment of atherosclerosis. The diagnosis of atherosclerosis risk factors was performed in accordance with the definitions provided by the Examination Committee of Criteria for the Metabolic Syndrome in Japan [20, 21]. Hypertension was defined as systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg; diabetes diagnosis was defined as a fasting plasma glucose level ≥110 mg/dL; and dyslipidemia was defined as a triglyceride level ≥150 mg/dL and/or HDL-cholesterol level <40 mg/dL.

2. 2. 4. Statistical analysis

Multicollinearity analyses were performed using SMI, age, and WC as variables. Explanatory variables with a low contribution rate were excluded from the analysis. Multiple linear regression analysis was performed to determine the relative contribution of explanatory variables to the response variable (number of risk factors), grouped by the presence or absence of WC criteria. To identify the optimal appendicular SMI for predicting at least two components of the metabolic syndrome, we performed receiver operating characteristic (ROC) analysis. The best cutoff value was determined by the Youden index. The other analyses are the same as described for study 1.

3. Results

3. 1. Study 1

The subject characteristics are presented in Table 1. The mean age, height, weight, and BMI were not significantly different between the validation group and the cross-validation group in both males and females.

According to the results of stepwise multiple regression analyses, the BI index of Zh, BSA, and gender were

Table 1. Physical characteristics of the subjects in study 1

	Males			Females		
	Validation group	Cross-validation group	P value	Validation group	Cross-validation group	P value
n	268	268		331	330	
Age (year)	39.2 ± 13.6	39.3 ± 13.7	0.92	39.7 ± 12.9	39.6 ± 12.7	0.97
Height (cm)	170.3 ± 6.2	170 ± 6.3	0.90	158 ± 5.6	158 ± 5.5	0.79
Weight (kg)	68.9 ± 12.2	68.5 ± 10.8	0.94	56.4 ± 10.1	56.2 ± 10.1	0.77
BMI (kg/m^2)	23.7 ± 3.7	23.7 ± 3.4	0.96	22.6 ± 3.9	22.5 ± 3.8	0.91

Values are presented as mean ± standard deviation.

selected as significant contributors for predicting the LSTM of upper limbs, and the BI index of Zw, age, and height were selected as significant contributors for predicting the LSTM of lower limbs. Regression analyses showed the prediction equation as follows:

LSTM of upper limbs (kg)
= (0.086 × BI index of Zh) + (0.518 × BSA)
+ (−0.520 × gender) − 2.115,
LSTM of lower limbs (kg)
= (0.143 × BI index of Zw) + (−0.035 × age)
+ (0.085 × height) − 9.541,
where age is in years. Gender for male = 1 and female = 2.

The relationship between the BIA-predicted and DXA-measured LSTM measurements in the validation group is shown in Table 2. There was a significant positive correlation between the LSTM measurements for upper and lower limbs predicted by BIA and the LSTM measurements performed using DXA (upper, r = 0.942, P < 0.001; lower, r = 0.950, P < 0.001).

The prediction equation derived from the validation group was used to predict LSTM measurements in the cross-validation group. There were significant correlations between measured and predicted LSTM values, respectively (Table 2). Analyses also showed that the LSTM values of upper and lower limbs predicted by BIA were significantly correlated with the LSTM measurements taken by DXA (upper, r = 0.944, P < 0.001; lower, r = 0.949, P < 0.001).

All data was pooled to generate the final regression equation:

LSTM of upper limbs (kg) = (0.088 × BI index of Zh)
+ (0.480 × BSA) + (−0.554 × gender) − 1.851,
LSTM of lower limbs (kg) = (0.144 × BI index of Zw)
+ (−0.032 × age) + (0.086 × height) − 9.877,
where age is in years. Gender for males = 1 and females = 2.

The r and standard error for estimating the regression equation for upper and lower limbs were 0.943 (P < 0.001), 0.950 (P < 0.001) and 0.42kg, 0.96kg, respectively (Table 2).

3. 2. Study 2

The subject characteristics are presented in Table 3. The mean height, body weight, BMI, and WC were sig-

Table 2. The correlation between LSTM estimated by BIA method and LSTM by DXA

	Validation group (n = 599)		Cross-validation group (n = 598)		All subjects (n = 1197)	
	Upper limbs	Lower limbs	Upper limbs	Lower limbs	Upper limbs	Lower limbs
r	0.942	0.950	0.944	0.949	0.943	0.950
SEE (kg)	0.50	0.96	0.47	0.94	0.42	0.96
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

SEE: Standard error of estimate

Table 3. Clinical characteristics of subjects in study 2

	Males	Females	P value
Number	998	163	
Age (year)	49.4 ± 7.4	48.2 ± 8.9	0.216
Height (cm)	171.4 ± 5.8	158.7 ± 5.2	<0.001
Weight (kg)	68.9 ± 9.1	57.3 ± 8.7	<0.001
BMI (kg/m^2)	23.4 ± 2.7	22.7 ± 3.3	<0.001
Waist circumference (cm)	84 ± 7.5	79.7 ± 8.9	<0.001
SBP (mmHg)	122.9 ± 15.6	112.6 ± 17	<0.001
DBP (mmHg)	78.3 ± 10	70.9 ± 11	<0.001
FPG (mg/dl)	102.9 ± 10.8	99.7 ± 10	<0.001
TG (mg/dl)	125.6 ± 102.1	85.7 ± 54.6	<0.001
HDL-C (mg/dl)	60.2 ± 14.6	67.8 ± 14.5	<0.001
LSTM upper and lower limbs (kg)	24.0 ± 2.3	16.5 ± 1.7	<0.001
upper limbs (kg)	6.1 ± 1.9	3.8 ± 0.6	<0.001
lower limbs (kg)	17.8 ± 2.3	12.8 ± 1.4	<0.001
SMI upper and lower limbs (kg/m^2)	8.2 ± 0.6	6.6 ± 0.5	<0.001
upper limbs (kg/m^2)	2.1 ± 0.2	1.5 ± 0.2	<0.001
lower limbs (kg/m^2)	6.0 ± 0.4	5,1 ± 0.4	<0.001
number of risk factors	0 431	118	
	1 373	33	
	2 160	9	
	3 34	3	

Values are presented as mean ± standard deviation.
SBP: systolic blood pressure, DBP: diastolic blood pressure, FPG: fasting plasma glucose, TG: triglyceride, HDL-C: HDL-cholesterol, LSTM: lean soft tissue mass, SMI: skeletal muscle index

Table 4. Results of the multiple linear regression analysis of the relationship between number of atherosclerosis risk factors and SMI, age, and waist circumference (WC)

	Males				Females			
	WC < 85 cm (n = 558)		WC ≥ 85 cm (n = 440)		WC < 90 cm (n = 142)		WC ≥ 90 cm (n = 21)	
	B	P value	B	P value	B	P value	B	P value
SMI_a	−0.066	0.136	0.070	0.186	−0.029	0.776	−0.011	0.961
Age	0.261	<0.001	0.177	<0.001	0.255	0.002	0.422	0.045
WC	0.235	<0.001	0.167	0.002	0.269	0.011	0.424	0.066

	Males				Females			
	WC < 85 cm (n = 558)		WC ≥ 85 cm (n = 440)		WC < 90 cm (n = 142)		WC ≥ 90 cm (n = 21)	
	B	P value	B	P value	B	P value	B	P value
SMI_u	−0.017	0.703	0.083	0.186	−0.136	0.141	0.039	0.859
Age	0.255	<0.001	0.175	<0.001	0.248	0.002	0.436	0.050
WC	0.215	<0.001	0.163	0.002	0.325	0.001	0.405	0.082

	Males				Females			
	WC < 85 cm (n = 558)		WC ≥ 85 cm (n = 440)		WC < 90 cm (n = 142)		WC ≥ 90 cm (n = 21)	
	B	P value	B	P value	B	P value	B	P value
SMI_l	−0.109	0.011	0.036	0.489	−0.105	0.233	0.040	0.850
Age	0.260	<0.001	0.177	<0.001	0.244	<0.001	0.440	0.045
WC	0.247	<0.001	0.183	0.001	0.300	0.001	0.411	0.065

Objective variable: number of risk factors, Explanatory variable: SMI_a or SMI_u or SMI_l, age, and WC
B: standardized partial regression coefficient, SMI_a: Skeletal muscle mass index of upper and lower limbs, SMI_u: Skeletal muscle mass index of upper limbs, SMI_l: Skeletal muscle mass index of lower limbs, WC: waist circumference

nificantly higher in the males compared to the females. There were no significant differences in the mean age between the males and females.

Table 4 shows the results of multiple linear regression analyses for determining the relationship between the number of atherosclerosis risk factors and SMI, age, and WC. There was multicollinearity between BMI measurements, and the contribution rate of BMI was lower than that of WC. Therefore, BMI was excluded from the analysis. The number of atherosclerosis risk factors was significantly correlated with the SMI of lower limbs (B = -0.164, P < 0.001) in males with WC < 85 cm. Whereas in males with other combinations, the number of risk factors was significantly correlated with age and WC, but not SMI. In females, there was no significant correlation between the number of risk factors and SMI.

We performed gender-specific ROC analyses to assess appendicular SMI as an indicator of at least two of the

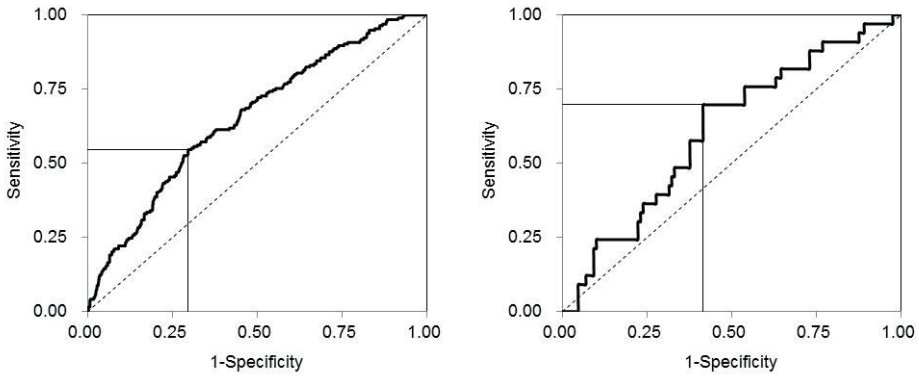

Fig 1. Gender-specific ROC for using SMI to detect the presence of at least two components of metabolic syndrome (raised TG and /or reduced HDL-C, raised BP, and raised FPG).

three components of metabolic syndrome (Figure 1). The sensitivity and the specificity of SMI cutoff values for males and females were 8.4 kg/m^2 and 6.5 kg/m^2, respectively. Furthermore, these cutoff values were higher than the cutoff of sarcopenia (7.0kg/m^2 for males and 5.7kg/m^2 for females) [8].

4. Discussion

In this study, we developed the first simple BIA device able to measure the skeletal muscle mass of the upper and lower limbs separately, and the prediction formula is disclosed. This study is the first report comparing risk factors for atherosclerosis and SMI, and determining the cutoff value of SMI for determining atherosclerosis. These results suggest that a decrease of skeletal muscle contributes to atherosclerosis risk earlier than that of sarcopenia in middle-aged subjects.

From the results of the study 1, where the prediction formulas derived from the validation groups were applied to the cross-validation groups, the LSTM values predicted by the BIA methods were strongly correlated with those measured using DXA. These results suggest that the BIA method used to measure the LSTM of upper and lower limbs is the simple and practical method for predicting LSTM.

From the results of the multiple regression analyses in study 2, it was suggested that WC and age had the strongest association with atherosclerosis risk factors among the males (WC< 85cm). Also, the SMI of the lower limbs was the second largest contributing factor next to WC and age, in the male subjects. However, in the female subjects, the number of risk factors was not significantly correlated with SMI. The reasons for the gender differences in the predictive variables might be due to the lower overall volume of muscle mass in the females compared to the males. Therefore, the contribution of muscle mass is lower in females than in males. A second factor contributing to this difference might be the influence of sex hormones. The male hormone testosterone has been shown to induce skeletal muscle protein anabolism and increase muscle size and strength [22]. Meanwhile, estrogen, a female hormone, has been associated with decreased atherosclerosis risk [23].

Skeletal muscle is the largest tissue in human body and plays an important role in energy metabolism, glucose uptake, and physical activity. Approximately 15% of the circulating blood volume is supplied to skeletal muscle at rest, and approximately 20% of the oxygen used in the body is consumed by skeletal muscle [24]. Glucose in the blood is carried to skeletal muscle, and metabolized in the presence of oxygen [24]. A previous study has reported that the muscles of the upper limbs, which carry the marginal gravitational load, show less adaptation compared to the muscles of the lower limbs after unloaded inactivity [25]. Muscle mass of lower limbs is greater than that of the upper limbs. Other previous studies have reported that the loss of skeletal muscle mass with aging was greater in the lower body compared to the upper body [26]. Therefore, it is assumed that skeletal muscles of the lower limbs are more important for motor and metabolic function compared to muscles of the upper limbs.

The exact mechanism by which the decrease in skeletal muscle mass leads to the development of atherosclerosis risk is not fully understood. It is possible that insulin resistance, which leads to decrease in skeletal muscle mass, also leads to the development of atherosclerosis risk factors such as diabetes, dyslipidemia, and hypertension [27]. Skeletal muscle is responsible for a major part of insulin-stimulated disposal of glucose in the body and it plays an important role in the pathogenesis of insulin resistance. Previous studies revealed that decrease in the skeletal muscle mass caused a decline and hypofunction of mitochondria in skeletal muscle [17, 28]. Skeletal muscle mitochondrial dysfunction is involved in the accumulation of intra-myocellular lipid metabolites. When this occurs, fatty acids in skeletal muscle are not metabolized, and it becomes an insulin resistance risk factor [28, 29]. As for future studies, it is necessary to explore the molecular mechanisms associated with the development of atherosclerosis risk that is associated with decreased skeletal muscle mass.

The BIA method for measuring the LSTM in the upper and lower limbs in this study has potentials for clinical applications [30-35]. Since our BIA method uses only two kinds of impedance, the total time required for measurement is about 5 seconds. The measurement system is simple, low-cost, and compact (it weighs approximately 2 kg and measures 30cm-square), and it would lead to an easy detection of decrease in skeletal muscle mass at home.

The device used in this study has some limitations. First, the BIA method, in general, it affected by the water

volume in the body, therefore dehydration and edema [36] or within-day variability may affect the results of the measurements [37]. Then, measured values may not be accurate in the subjects with edema or in the dialysis subjects.

Considering within-day variability, our BIA device did not previously show within-day variability [37]. However, it may be preferable to measure the impedance at regularly scheduled times for accuracy.

Second, with the measuring position, it is not adaptable for those who cannot keep a standing position.

In addition, we have to consider the other limitations. First, the participants in this study were only Japanese people.

Second, the participants were enrolled so that each generation became almost equal, therefore, the participant group has few ratios of the elderly person who may be develop sarcopenia.

Third, we did not evaluate the functional aspects of the skeletal muscle, such as muscle strength, and exercise habits. Muscle strength training has been reported to reduced metabolic syndrome risk [38]. Further studies on the evaluation of muscle strength based on the criteria for diagnosing sarcopenia should be performed.

In conclusion, the BIA method for predicting LSTM presented in this study are accurate and simple , then may be useful for assessing the muscle mass of upper and lower limbs. Therefore, a new device using the skeletal muscle mass prediction formula for the upper and lower limbs will make it probable to determine the extent of sarcopenia and to predict atherosclerosis risk at home.

Conflict of interest statement

Tetsuya Sato is an employee of OMRON HEALTHCARE Co., Ltd. The other authors declare no conflict of interest.

Ethical statement

Study 1

Informed consent was obtained from each study subject, and this study was approved by the research ethics committee of OMRON Healthcare Co., Ltd. (Approval number OHQ-GK-03096).

Study 2

Informed consent was obtained from each study subject, and this study was approved by the research ethics committee of Kyoto Women's University (Approval number 25-26).

References

[1] Rosenberg IH: Sarcopenia: Origins and clinical relevance. *J Nutr.*, **127**, 990S-991S (1997)

[2] Kuzuya M: Impact of sarcopenia and frailty on preventive care for older people. *Intern Med*, **106**, 557-561 (2017) (in Japanese)

[3] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al: Sarcopenia: European consensus on definition and diagnosis: Report of the European working group on sarcopenia in older people. *Age Ageing*, **39**, 412-423 (2010)

[4] Mijnarends DM, Meijers JMM, Halfens RJG, Borg S, Luiking YC, Verlaan S, et al: Validity and reliability of tools to measure muscle mass, strength, and physical performance in community-dwelling older people: a systematic review. *J Am Med Dir Assoc*, **14**, 170-178 (2013)

[5] Woods JL, Iuliano-Burns S, King SJ, Strauss BJ, Walker KZ: Poor physical function in elderly women in low-level aged care is related to muscle strength rather than to measures of sarcopenia. *Clin Interv Aging*, **6**, 67-76 (2011)

[6] Liu LK, Lee WJ, Liu CL, Chen LY, Lin MH, Peng LN, et al: Age-related skeletal muscle mass loss and physical performance in Taiwan: implications to diagnostic strategy of sarcopenia in Asia. *Geriatr Gerontol Int*, **13**, 964-971 (2013)

[7] Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, et al: Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol*, **147**, 755-763 (1998)

[8] Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al: Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc, 15, 95-101 (2014)

[9] Kaido T, Uemoto S: Direct segmental multi-frequency bioelectrical impedance analysis is useful to evaluate Sarcopenia. *Am J Transplant*, **13**, 2506-2507 (2013)

[10] Lu CW, Yang KC, Chang HH, Lee LT, Chen CY, Huang KC: Sarcopenic obesity is closely associated with metabolic syndrome. *Obes Res Clin Pract*, **7**, e301-e307 (2013)

[11] Seino S, Shinkai S, Iijima K, Obuchi S, Fujiwara Y, Yoshida H, et al: Reference values and age differences in body composition of community-dwelling older Japanese men and women: a pooled analysis of four cohort studies. *PloS one*, **10**, e0131975 (2015)

[12] Dodds RM, Granic A, Davies K, Kirkwood TB, Jagger C, Sayer AA: Prevalence and incidence of sarcopenia in the very old: findings from the Newcastle 85+ Study. *J Cachexia Sarcopenia Muscle*, **8**, 229-237 (2017)

[13] Çeliker M, Selçuk MY, Olt S: Sarcopenia in diabetic nephropathy: a cross-sectional study. *Rom J Intern Med*, **1**, 1-15 (2018)

[14] Yamada M, Yamada Y, Arai H: Comparability of two representative devices for bioelectrical impedance data acquisition. *Geriatr Gerontol Int*, **16**, 1087-1088 (2016)

[15] Kohara, K: Sarcopenic obesity in aging population: current status and future directions for research. *Endocrine*, **45**, 15-25 (2014)

[16] Moon SS: Low skeletal muscle mass is associated with insulin resistance, diabetes, and metabolic syndrome in the Korean population: The Korea National Health and Nutrition Examination Survey (KNHANES) 2009-2010. *Endocr J*, **61**, 61-70 (2014)

[17] Sato T, Kanaji K, Nishikawa H, Miyawaki T: Relationships of skeletal muscle mass and visceral fat with atherosclerosis risk factors in middle-aged Japanese people: An assessment using accurate, simple bioelectrical impedance methods. *Ningen Dock Int*, **5**, 15-21 (2018)

[18] Fujimoto S, Watanabe T, Sakamoto A, Yukawa K, Morimoto K: Studies on the physical surface area of Japanese. 18. Calculation formulas in three stages over all ages. *Nippon Eiseigaku Zasshi*, **23**, 443-450 (1968) (In Japanese with English summary).

[19] Oshima Y, Shiga T, Namba H, Kuno S: Estimation of whole-body skeletal muscle mass by bioelectrical impedance analysis in the standing position. *Obes Res Clin Pract*, **4**, e1-e7 (2010)

[20] Miyawaki T, Hirata M, Moriyama K, et al: Metabolic syndrome in Japanese diagnosed with visceral fat measurement by computed tomography. *Proc Japan Acad*, **81**, 471-479 (2005)

[21] The examination committee of criteria for metabolic syndrome. Definition and criteria of metabolic syndrome. *J Jpn Soc Int Med*, **94**, 794-809 (2005) (in Japanese)

[22] Gallagher D, Visser M, De Meersman RE, Sepúlveda D, Baumgartner RN, Pierson RN, et al: Appendicular skeletal muscle mass: effects of age, gender, and ethnicity. *J of Appl Physiol*, **83**, 229-239 (1997)

[23] Mendelsohn ME, Karas RH: The protective effects of estrogen on the cardiovascular system. *N Engl J Med*, **340**, 1801-1811 (1999)

[24] Rowell LB: Human Cardiovascular Control. New York, NY, USA, *Oxford University Press*, **1993**, 205 (1993)

[25] LeBlanc A, Gogia P, Schneider V, Krebs J, Schonfeld E, Evans H: Calf muscle area and strength changes after five weeks of horizontal bed rest. *Am J Sports Med*, **16**, 624-629 (1988)

[26] Janssen I, Heymsfield SB, Wang ZM, Ross R: Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. *J Appl Physiol*, **89**, 81-88 (2000)

[27] Lim S, Kim JH, Yoon JW, et al: Sarcopenic obesity: prevalence and association with metabolic syndrome in the Korean Longitudinal Study on Health and Aging (KLoSHA). *Diabetes Care*, **33**, 1652-1654 (2010)

[28] Lee CG, Boyko EJ, Strotmeyer ES: Association between Insulin resistance and lean mass loss and fat mass gain in older men without diabetes mellitus. *J Am Geriatr Soc*, **59**, 1217-1224 (2011)

[29] Brands M, Verhoeven AJ, Serlie MJ: Role of mitochondrial function in insulin resistance. *Adv Exp Med Biol*, **942**, 215-234 (2012)

[30] Makwana K, Kalasava K, Ghori V: Evaluate cardiovascular risk factor in Indian insulin sensitive & resistant subjects using lipid profile & visceral fat measurement. *Int J Diabetes Res*, **1**, 87-91 (2012)

[31] Sanghani NB, Parchwani DN, Palandurkar KM, Shah AM, Dhanani JV: Impact of lifestyle modification on glycemic control in patients with type 2 diabetes mellitus. *Indian J Endocrinol Metab*, **17**, 1030-1039 (2013)

[32] Grande AJ, Silva V, Parra SA: Effectiveness of exercise at workplace in physical fitness: uncontrolled randomized study. *Einstein*, **12**, 55-60 (2014)

[33] Heger Z, Gumulec J, Ondrak A, Skoda J, Zitka Z, Cernei N, et al: Influence of long-distance bicycle riding on serum/urinary biomarkers of prostate cancer. *Int J Mol Sci*, **17**, 377 (2016)

[34] Bhutani S, Klempel MC, Berger RA, Varady KA: Improvements in coronary heart disease risk indicators by alternate ― Day fasting involve adipose tissue modulations. *Obesity*, **18**, 2152-2159 (2010)

[35] Cramer H, Thoms MS, Anheyer D, Lauche R, Dobos G: Yoga in women with abdominal obesity ― A randomized controlled trial. *Dtsch Arztebl Int*, **113**, 645 (2016)

[36] Hutcheson L, Hutcheson L, Berg KE, Prentice E: Body impedance analysis and body water loss. *Res Q Exerc Sport*, **59**, 359-362 (1988)

[37] Oshima Y, Shiga T: Within-day variability of whole-body and segmental bioelectrical impedance in a standing position. *Eur J Clin Nutr*, **60**, 938-941 (2006)

[38] Wijndaele K, Duvigneaud N, Matton L, Duquet W, Thomis M, Beunen G, et al: Muscular strength, aerobic fitness, and metabolic syndrome risk in Flemish adults. *Med Sei Sports Exerc*, **39**, 233-240 (2007)

和文抄録

目的：本研究は，生体インピーダンス（BI）法を用いて，上肢および下肢それぞれの骨格筋量の推定式を搭載した機器を開発し，動脈硬化リスク因子との関係を調査することを目的とした。

方法：研究1として，20～80歳の健康な男女1197名のデータを用いて，上肢および下肢の骨格筋量の推定式を開発した。各々の被験者は，生体インピーダンス，身長および体重を測定し，骨格筋量のリファレンスは二重エネルギーX線吸収測定法（DXA）を用いて測定した。研究2として，未治療の男女の人間ドック健診受診者1161人を対象として，前記で開発した骨格筋量の推定式をインストールした装置を用いて上肢および下肢の骨格筋量を推定し，腹囲および動脈硬化リスク因子も測定した。次に，上肢および下肢の骨格筋量から骨格筋量指数（SMI）を算出し，目的変数を動脈硬化リスク数，独立変数をSMI，年齢，および腹囲とし重回帰分析を行った。さらに，動脈硬化リスク数が2以上となる上下肢SMIのカットオフ値をROC解析を用いて求めた。

結果：研究1では，骨格筋量の推定値とリファレンスのDXAの相関係数は上肢と下肢がそれぞれ0.94と0.95（$P< 0.001$）であった。研究2では，腹囲が基準値の85cm未満の男性において，下肢のSMIの減少は動脈硬化リスク数の有意な寄与因子であった（$B = -0.109$, $P = 0.011$）。また，動脈硬化リスクが2個以上となる上下肢SMIのカットオフ値は男女それぞれ8.4kg/m^{2}と6.5kg/m^{2}であり，サルコペニア診断基準のカットオフ値（男性：7.0kg/m^2，女性：5.7kg/m^2）より高値であった。

結論：今回作成した推定式は，上肢および下肢それぞれの骨格筋量を高い精度で推定することが可能であった。動脈硬化リスクを評価する体組成の測定においては，従来のBMIや内臓脂肪蓄積の評価に加えて，上下肢別にSMIを評価することが重要であると考えられた。骨格筋の減少に伴い，動脈硬化リスクはサルコペニアリスクより早期に生じる可能性が示唆された。